

Claims

We claim:

1. An organic/inorganic composite comprising an organic fluid-swellaable, fibrous matrix and an inorganic mineral phase, wherein said inorganic mineral phase is deposited on and absorbed within said fluid-swellaable, fibrous matrix when said inorganic mineral phase is in the form of a liquid phase mineral precursor, and wherein said inorganic mineral phase is aligned along the long axis of each of the fibers of said fluid-swellaable, fibrous matrix that said inorganic mineral phase is deposited.
2. The organic/inorganic composite of claim 1, wherein the fibers of said fluid-swellaable, fibrous matrix are substantially parallel to one another.
3. The organic/inorganic composite of claim 1, wherein said fluid-swellaable, fibrous matrix comprises an interior with interstitial space, and wherein said inorganic mineral phase is absorbed into said interstitial space when said inorganic mineral phase is in the form of a liquid phase mineral precursor, which subsequently solidifies.
4. The organic/inorganic composite of claim 3, wherein said fluid-swellaable, fibrous matrix further comprises an exterior, and wherein said inorganic liquid-phase mineral precursor is absorbed into said interstitial space and is coated on said exterior of said fluid-swellaable, fibrous matrix.
5. The organic/inorganic composite of claim 4, wherein said inorganic liquid-phase mineral precursor deposited on said fluid-swellaable, fibrous matrix has a non-faceted topography when said liquid-phase mineral precursor becomes solidified.
6. The organic/inorganic composite of claim 1, wherein said inorganic mineral phase comprises hydroxyapatite crystals oriented in the [001] direction along the long axis of each of the fibers of said fluid swellaable, fibrous matrix.

7. The organic/inorganic composite of claim 1, wherein said inorganic mineral phase has an amorphous morphology or crystalline morphology.

8. The organic/inorganic composite of claim 1, wherein said fluid-swellaable, fibrous matrix comprises at least one material selected from the group consisting of collagen, elastin, chitin, cellulose, chitosan, and peptide nanofibers.

9. The organic/inorganic composite of claim 1, wherein said fluid-swellaable, fibrous matrix has been surfaced-modified.

10. The organic/inorganic composite of claim 1, wherein said fluid-swellaable, fibrous matrix has been surface modified using a method selected from the group consisting of plasma treatment, etching, ion implantation, radiation, electron beam, chemical functionalization, grafting, photopolymerization, and adsorption.

11. The organic/inorganic composite of claim 1, wherein said fluid-swellaable, fibrous matrix comprises collagen.

12. The organic/inorganic composite of claim 11, wherein said collagen is selected from the group consisting of collagen type 1, collagen type 2, collagen type 3, collagen type 4, collagen type 5, collagen type 6, collagen type 7, collagen type 8, collagen type 9, collagen type 10, collagen type 11, collagen type 12, collagen type 13, collagen type 14, collagen type 15, collagen type 16, collagen type 17, collagen type 18, collagen type 19, and collagen type 20, or combinations thereof.

13. The organic/inorganic composite of claim 11, wherein said collagen comprises collagen fibers, wherein each of said fibers comprises abutting fibrils with gaps arranged between said abutting fibrils, and wherein said liquid-phase mineral precursor is absorbed into said gaps by capillarity, and wherein said inorganic mineral phase is aligned along the long axis of each of said fibrils.

14. The organic/inorganic composite of claim 11, wherein said collagen has been surface modified.

15. The organic/inorganic composite of claim 1, wherein said inorganic mineral phase comprises at least one member selected from the group consisting of calcium phosphate, calcium carbonate, hydroxyapatite, strontium carbonate, calcium sulfate, calcium oxalate, magnesium-bearing calcium carbonate, and magnesium-bearing calcium phosphate.

16. The organic/inorganic composite of claim 1, wherein said inorganic mineral phase comprises at least one member selected from the group consisting of hydroxyapatite, octacalcium phosphate, tricalcium phosphate, carbonated hydroxyapatite, fluorinated hydroxyapatite, brushite, magnesium containing hydroxyapatite, dicalcium phosphate dihydrate, and amorphous calcium phosphate.

17. The organic/inorganic composite of claim 1, wherein said inorganic mineral phase comprises hydroxyapatite crystals oriented in the [001] direction along the long axis of each of the fibers of said fluid-swellaable fibrous matrix.

18. The organic/inorganic composite of claim 1, wherein said fluid-swellaable, fibrous matrix comprises collagen fibers, wherein each of said fibers comprises abutting fibrils, and wherein said inorganic mineral phase comprises hydroxyapatite crystals oriented in the [001] direction along the long axis of each of said collagen fibers and each of said fibrils.

19. The organic/inorganic composite of claim 1, wherein said composite further comprises one or more biologically active agents.

20. The organic/inorganic composite of claim 19, wherein said one or more biologically active agents are selected from the group consisting of medicaments; vitamins; mineral supplements; substances used for the treatment, prevention, diagnosis, cure or mitigation of disease or illness; substances affecting the structure or function of the body; drugs; antimicrobial agents; antifungal agents; antibacterial agents; antiviral agents; antiparasitic agents; growth

factors; angiogenic factors; anaesthetics; mucopolysaccharides; metals; cells; acid mucopolysaccharides; proteins; enzymes, peptides; and wound healing agents.

21. The organic/inorganic composite of claim 20, wherein said one or more biologically active agents are seeded on said composite or embedded within said composite.

22. The organic/inorganic composite of claim 20, wherein said one or more biologically active agents are pendants attached to said organic fluid-swellable, fibrous matrix or said inorganic mineral phase.

23. The organic/inorganic composite of claim 20, wherein said one or more biologically active agents are embedded within said organic fluid-swellable, fibrous matrix, or said inorganic mineral phase, or both.

24. The organic/inorganic composite of claim 1, wherein said organic/inorganic composite is in a form selected from the group consisting of an injectable liquid, a malleable paste, a malleable putty, a particulate, a film, a molded solid, and a preformed solid.

25. The organic/inorganic composite of claim 3, wherein said liquid phase precursor crystallizes in said interstitial space in said fluid-swellable matrix.

26. The organic/inorganic composite of claim 11, wherein said collagen comprises a plurality of substantially parallel fibers, wherein said inorganic mineral phase is absorbed into said plurality of parallel fibers, and wherein crystals of said inorganic mineral phase are embedded within the organic matrix.

27. The organic/inorganic composite of claim 1, wherein said organic/inorganic composite is porous.

28. The organic/inorganic composite of claim 27, wherein said pores range from about 50 microns to about 500 microns or more in diameter.

29. The organic/inorganic composite of claim 1, wherein said organic fluid-swellaable, fibrous matrix is porous.

30. The organic/inorganic composite of claim 27, wherein the microporosity is generated using freeze-drying techniques, supercritical processing, porogens, soluble salts or molecular compounds, phase segregating polymers, or high temperature sintering.

31. The organic/inorganic composite of claim 1, wherein said organic substrate is biocompatible and bioresorbable.

32. The organic/inorganic composite of claim 1, wherein said fluid-swellaable matrix comprises a scaffold seeded with cells.

33. The organic/inorganic composite of claim 32, wherein cells are selected from the group consisting of bone marrow stem cells, osteoblasts, osteoclasts, osteocytes, blood cells, epithelial cells, odontoblasts, ameloblasts, cementoblasts, and neural cells.

34. The organic/inorganic composite of claim 1, wherein said organic fluid-swellaable matrix comprises a film.

35. The organic/inorganic composite of claim 1, wherein said composite comprises a plurality of said organic substrates arranged as lamellae.

36. The organic/inorganic composite of claim 35, wherein said lamellae are arranged concentrically around a central void, in an osteon-like structure.

37. The organic/inorganic composite of claim 1, wherein said composite comprises a plurality of said organic fluid-swellaable matrices, and wherein said composite further comprises an adhesive layer between each of said organic fluid-swellaable matrices.

38. The organic/inorganic composite of claim 37, wherein said plurality of organic substrates have a parallel orientation.

39. The organic/inorganic composite of claim 37, wherein said plurality of organic substrates are arranged in an alternating orientation.

40. A process for making organic/inorganic composites, said method comprising contacting an acidic polymer with a mineralizing solution under conditions suitable to form an inorganic liquid-phase mineral precursor, and contacting said inorganic liquid-phase mineral precursor with an organic fluid-swellable, fibrous matrix, wherein said inorganic liquid-phase mineral precursor is absorbed into, and subsequently hardens within, said fluid-swellable, fibrous matrix, and wherein said hardened inorganic liquid-phase mineral precursor is aligned along the long axis of each of the fibers of said fluid-swellable, fibrous matrix to which said precursor is contacted.

41. The process according to claim 40, wherein said acidic polymer has a molecular weight in the range of about 1000 to about 100,000 g/mol.

42. The process according to claim 40, wherein said second contacting step is repeated until said organic fluid-swellable matrix is sufficiently mineralized.

43. The process according to claim 40, wherein said acidic polymer comprises at least one member selected from the group consisting of polyacrylic acid, polymethacrylic acid, sulfonated polymers, phosphorylated proteins or peptides, phosphorylated polymers, sulfated polysaccharides, sulfated glycoproteins, polyaspartic acid, polyglutamic acid, polyaspartate, polyvinyl phosphate, and polyvinyl phosphonate, or combinations thereof.

44. The process according to claim 40, wherein said fluid-swellable, fibrous matrix comprises a material selected from at least one member of the group consisting of collagen, elastin, chitin, chitosan, cellulose, and peptide nanofibers.

45. The process according to claim 40, wherein said fluid-swellable, fibrous matrix comprises collagen fibers.

46. The process according to claim 40, wherein said collagen is selected from the group consisting of collagen type 1, collagen type 2, collagen type 3, collagen type 4, collagen type 5, collagen type 6, collagen type 7, collagen type 8, collagen type 9, collagen type 10, collagen type 11, collagen type 12, collagen type 13, collagen type 14, collagen type 15, collagen type 16, collagen type 17, collagen type 18, collagen type 19, and collagen type 20, or combinations thereof.

47. The process according to claim 40, wherein said inorganic liquid-phase mineral precursor comprises at least one member selected from the group consisting of calcium phosphate, calcium carbonate, hydroxyapatite, strontium carbonate, and calcium sulfate, calcium oxalate, magnesium-bearing calcium carbonate, and magnesium-bearing calcium phosphate.

48. The process according to claim 40, wherein said inorganic liquid-phase mineral precursor comprises at least one member selected from the group consisting of hydroxyapatite, octacalcium phosphate, tricalcium phosphate, carbonated hydroxyapatite, fluorinated hydroxyapatite, brushite, magnesium containing hydroxyapatite, dicalcium phosphate dihydrate, and amorphous calcium phosphate.

49. The process according to claim 40, wherein said method further comprises associating a biologically active agent within said composite.

50. The process according to claim 49, wherein said biologically active agents comprise at least one member selected from the group consisting of medicaments; vitamins; mineral supplements; substances used for the treatment, prevention, diagnosis, cure or mitigation of disease or illness; substances affecting the structure or function of the body; drugs; antimicrobial agents; antifungal agents; antibacterial agents; antiviral agents; antiparasitic agents; growth factors; angiogenic factors; anaesthetics; mucopolysaccharides; metals; cells; acid mucopolysaccharides; proteins; enzymes, peptides; and wound healing agents.

51. The process according to claim 40, wherein said inorganic liquid-phase mineral precursor is formed by combining calcium salt and said acidic polymer to form an aqueous solution, and reacting said aqueous solution with ammonium carbonate vapor or ammonium phosphate vapor.

52. The process according to claim 51, wherein the aqueous solution is reacted with the ammonium carbonate vapor, and wherein the ammonium carbonate vapor is provided through the decomposition of at least one ammonium carbonate material selected from the group consisting of ammonium carbonate monohydrate, ammonium carbonate dihydrate, and ammonium carbamate.

53. The process according to claim 51, wherein the aqueous solution is reacted with the ammonium phosphate vapor, and wherein the ammonium phosphate vapor is provided through the decomposition of at least one ammonium phosphate material selected from the group consisting of ammonium phosphate monobasic, ammonium phosphate dibasic.

54. The process according to claim 40, wherein said inorganic liquid-phase mineral precursor is formed by combining calcium chloride and a combination of acidic polymers to form an aqueous solution, and reacting said aqueous solution with ammonium phosphate vapor.

55. The process according to claim 40, wherein said inorganic liquid-phase mineral precursor is formed by combining calcium chloride and a combination of acidic polymers to form an aqueous solution, and reacting said aqueous solution with a phosphate containing solution.

56. The process according to claim 40, wherein said inorganic liquid-phase mineral precursor is formed by combining calcium salt and a combination of acidic polymers to form an aqueous solution, and reacting said aqueous solution with phosphate generated by enzymatic degradation of phosphate containing compounds.

57. The process according to claim 40, wherein said inorganic liquid-phase mineral precursor is formed by combining calcium salt and ammonium phosphate, and a combination of acidic polymers to form an aqueous solution, in which precipitation is caused by a change of temperature, change of pH, evaporation, or removal of crystallization inhibitor.

58. The process according to claim 40, wherein said fluid-swellaable, fibrous matrix comprises an exterior surface and an interior containing an interstitial space, wherein said inorganic liquid-phase mineral precursor is absorbed into said interstitial space of said fluid-swellaable, fibrous matrix, and deposited onto said exterior surface of said fluid-swellaable, fibrous matrix; and wherein said liquid-phase mineral precursor deposited onto said exterior surface of said fluid-swellaable matrix has a non-faceted topography when solidified.

59. An organic/inorganic composite made according to the process of claim 40.

60. The organic/inorganic composite of claim 59, wherein said fluid-swellaable, fibrous matrix comprises a material selected from the group consisting of collagen, elastin, chitin, chitosan, cellulose, and peptide nanofibers; and wherein said inorganic liquid-phase mineral precursor is selected from the group consisting of calcium phosphate, calcium carbonate, hydroxyapatite, strontium carbonate, calcium sulfate, calcium oxalate, magnesium-bearing calcium carbonate, and magnesium-bearing calcium phosphate, or combinations thereof.

61. The organic/inorganic composite of claim 59, wherein said inorganic liquid-phase mineral precursor comprises at least one member selected from the calcium phosphate group consisting of hydroxyapatite, octacalcium phosphate, tricalcium phosphate, carbonated hydroxyapatite, fluorinated hydroxyapatite, brushite, magnesium containing hydroxyapatite, dicalcium phosphate dihydrate, and amorphous calcium phosphate.

62. A method for treating a bone defect comprising applying an organic/inorganic composite to the site of the bone defect, wherein said organic/inorganic composite comprises a fluid-swellaable, fibrous matrix and an inorganic mineral phase, and wherein said inorganic mineral phase is absorbed into said fluid-swellaable, fibrous matrix when said inorganic mineral

phase is in the form of a liquid-phase mineral precursor, which subsequently solidifies and is aligned along the long axis of each of the fibers of said fluid-swellable, fibrous matrix to which said inorganic mineral phase is absorbed.

63. The method according to claim 62, wherein said organic/inorganic composite is applied as an injectable liquid, a film, a malleable putty, a malleable paste, a particulate, or a molded or preformed solid.

64. The method according to claim 62, wherein said fluid-swellable, fibrous matrix comprises a material selected from the group consisting of collagen, elastin, chitin, chitosan, cellulose, and peptide nanofibers.

65. The method according to claim 62, wherein said inorganic mineral is selected from the group consisting of calcium phosphate, calcium carbonate, hydroxyapatite, strontium carbonate, and calcium sulfate, calcium oxalate, magnesium-bearing calcium carbonate, and magnesium-bearing calcium, or combinations thereof.

66. The method according to claim 62, wherein said organic/inorganic composite further comprises a biologically active agent.

67. The method according to claim 62, wherein said organic/inorganic composite is porous.

68. The method according to claim 62, wherein said organic substrate is biocompatible and bioresorbable.

69. The method according to claim 62, wherein said fluid-swellable, fibrous matrix comprises a scaffold seeded with cells.

70. The method according to claim 69, wherein said cells are selected from the group consisting of bone marrow stem cells, osteoblasts, osteoclasts, osteocytes, blood cells, epithelial cells, odontoblast, ameloblasts, and neural cells, or combinations thereof.

71. The method according to claim 62, wherein said fluid-swellable, fibrous matrix is a film.

72. The method according to claim 62, wherein said organic/inorganic composite comprises a plurality of said fluid-swellable, fibrous matrices arranged as laminae.

73. The method according to claim 72, wherein said lamellae are arranged concentrically around a central void for passage of endogenous or exogenous cells.

74. The method according to claim 62, wherein said organic/inorganic composite comprises a plurality of said fluid-swellable, fibrous matrices, and wherein said organic/inorganic composite further comprises an adhesive layer between each of said organic substrates.

75. The method according to claim 74, wherein said plurality of organic substrates have a parallel orientation.

76. The method according to claim 74, wherein said plurality of organic substrates are in an alternating orientation.